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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,389	05/18/2001	Carl R. Alving	182.0010/WRAIR00-26	3181

7590

08/26/2003

ATTN: MCMR-JA (Ms Elizabeth Arwine)
Office of the Staff Judge Advocate US Army Researc
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER

CHEU, CHANGHWA J

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/859,389

Applicant(s)

ALVING ET AL.

Examiner

Jacob Cheu

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 19-21 is/are pending in the application.
- 4a) Of the above claim(s) 13, 14 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-12, 15-17, 20 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's amendment filed on June 24, 2003 has been received, entered into record and considered. The following information provided in the amendment affects the instant application:

1. Claim 18 is cancelled.
2. Claims 1-12, 12, 15-17, 20-21 are amended and currently under examination.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-12, 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, line 10, "with little or no cross reactivity" is vague and indefinite. It is unclear to what extent "little" is constituted.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in-

- (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
- (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-4, 8, 10-12, 17, 18 and 20-21 are rejected under 35 U.S.C. 102 (e) as anticipated by Asa et al.. (USP 6214566)

Asa teach measuring anti-squalene antibody by immobilizing squalene on the solid support, i.e. polystyrene (claim 1, 6), washing with blocking buffer (i.e. phosphate buffer saline, goat serum, See Example 3), contacting the immobilized squalene with test sample containing anti-squalene antibody to form an antibody complex (claim 1), and contacting the complex with a IgG having specificity to the antibody complex (See Example 3) and use immunoenzymatic detection, i.e. hydrogen peroxidase, to determine the presence of the squalene antibody. (See Example 6) Asa et al. disclose that using squalene-containing vaccine has been conducted in human subjects. (See Col. 4, line 10-50)

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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4. Claims 5-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asa et al. in view of Rodkey et al. (USP 6191108) and Lombardo et al. (USP 6166050)

Asa et al. reference ^{goat serum} has been discussed but fails specifically teaching using bovine serum albumins, human serum or mouse serum as blocking agents. Rodkey et al. teach using bovine serum and human serum as blocking agents for reducing non-specific binding of antibody-antigen. (Col. 11, line 35-37; Col. 40, line 52-55) Lombardo et al. teach using mouse serum as blocking agents. (Col. 35, line 10-12) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Asa et al. with different alternative blocking agents as taught by Rodkey et al. and Lombardo et al. because it is a routine practice in the art in reducing non-specific bindings in the immunoassay.

As to the range of bovine serum albumin claimed in claim 5 and 6, the Office takes the position that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges of the agents involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

5. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Asa et al. in view of Barchfeld et al.. (USP 5709879)

Asa reference has been discussed but fails to specifically teach using liposomes containing squalene. Barchfeld et al. teach using emulsion-liposome containing squalene in yielding a higher antibody response. (Col. 22, line 36-47) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Asa et al. with the liposome containing squalene as taught by Barchfeld et al, in order to result in a better immunoresponse.

Response to Applicant's argument

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6. Applicant points out that the instant invention differs from the reference of Asa et al. in that the instant invention recites a more specific specificity in binding with squalene, whereas the prior art does not specify this feature. Applicant also amends claim 1 incorporates two features, i.e. "squalene antibodies capable of specific binding with squalene" and "specific antibody complex with little or no cross reactivity", attempting to overcome the anticipatory rejections under Asa et al. Applicant's argument has been considered but is not convincing. Examiner would like to draw applicant's attention to claim 1 of the Asa et al. patent where Asa et al. teach a method of detecting antisqualene antibody in a sample by contacting the test sample with the antisqualene antibody to form a complex. The antisqualene inherently encompass both polyclonal and monoclonal antisqualene antibodies since both can form immunological complex when interact with the immobilized squalene. Accordingly, using alternative blocking agents as recited in claims 5-7 and 9 would have been obvious to one of ordinary skill in the art to use since it involves only routine practice in the art to reduce the non-specific binding in immunoassay.

With respect to claim 16, applicant argues that (1) Barchfeld et al. teach combining the liposomes and antigen "prior to mixing with emulsion" and (2) Asa et al. teach using distilled water for dilution which is inconsistent with the hydrophobic characteristics of the squalene. Therefore, it would have been a "disordered" result when incorporates the squalene into liposome as taught by Barchfeld et al. Applicant's arguments have been considered but are not persuasive. First, claim 16 further limits the *composition* recited in claim 15. There is no significant difference whether "prior to" or "thereafter" mixing the antigen with the liposomes

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since the purpose is merely to increase immunoresponse. Second, the Office takes the position that the issued US Patents are presumably valid. One in the art would optimize the emulsion process by using suitable organic solvent other than water, e.g. Tween, since using other emulsion agents for optimal results only involves routine practice in the art when encountering a similar situation.

With respect to claim 20, applicant argues that Asa et al. do not disclose, or suggest an assay for detecting antibody induced by injection of squalene. Applicant's argument is considered but is not convincing. Asa et al. disclose that using squalene-containing *vaccine* has been conducted in human subjects. (See Col. 4, line 10-50) Clearly, Asa et al. reference inherently anticipates its application to detect those subjects containing antisqualene antibody in their bodies.

Conclusion

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period

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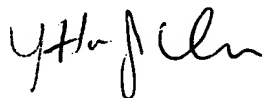
will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 9:00-5:00.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Job Cheu
Examiner
Art Unit 1641



August 14, 2003



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

8/22/03